AR201-13356A

Phosphoric Acid Derivatives
Category Justification and Testing Rationale

CAS Nos. 78-42-2 and 12645-31-7 (HPV Chemicals)
107-66-4, 126-73-8 and 298-07-7 (Supporting Chemicals)

Phosphoric Acid Derivatives Panel
American Chemistry Council

December, 2001

List of Member Companies in the Phosphoric Acid Derivatives Panel

The Phosphoric Acid Derivatives Panel of the American Chemistry Council includes the following member companies: Baker Petrolite Corporation, Bayer Corporation, Noveon, Inc. (formerly BF Goodrich), Crompton Corporation, and ICI Americas (Uniqema).

Executive Summary

The American Chemistry Council's Phosphoric Acid Derivatives (PAD) Panel, and its member companies, hereby submit for review and public comment their test plan for the Phosphoric Acid Derivatives category of chemicals under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Chemical Challenge Program.

As discussed in the report that follows, PAD chemicals are used primarily as flame retardant platicizers for polyvinylchloride resins, cellulose esters, lacquers and plastics, contributing flexibility and resistance to degradation at low temperatures. They are used as solvents in liquid-liquid extractions, and as intermediates for wetting agents and detergents, as well as anti-foaming agents. They are used extensively as dispersing agents in plastisols, as catalysts in the manufacture of phenolic and urea resins, and in metal separation and extraction. These chemicals are also used as heat exchange mediums (2000 Chemical Economics Handbook).

All chemicals in this category are alkyl esters of phosphoric acid and have been reviewed by the GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance (BUA, 1992) as a category. Existing data for members of this category indicate that they are of low concern for aquatic and mammalian toxicity, will partition to soil and sediment, and are not readily biodegradable. We conclude that there is sufficient data on the members of this category to meet requirements of the HPV Challenge Program and no additional testing is proposed.

Phosphoric Acid Derivatives Category

Relying on several factors specified in EPA's guidance document on "Development of Chemical Categories in the HPV Challenge Program," in which use of chemical categories is encouraged, the following closely related chemicals constitute a chemical category:

Tris(2-ethylhexyl) phosphate	(78-42-2)
2-Ethylhexyl phosphate	(12645-31-7)
Dibutyl hydrogen phosphate	(107-66-4)*
Tributyl phosphate	(126-73-8)*
Bis(2-ethylhexyl) hydrogen phosphate	(298-07-7)*

**Not sponsored as part of the EPA HPV Challenge Program. Used for data purposes only.*

Structural Similarity.

A key factor supporting the classification of these chemicals as a category is their structural similarity. All chemicals in this category are alkyl esters of phosphoric acid (See **Figure 1**). The GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance reviewed the alkyl phosphate esters as a category in 1992 (BUA, 1992).

Metabolism.

"In mammalian metabolism, the phosphoric acid tri-esters are, as a rule, rapidly degraded to the corresponding di-ester. Only a small amount is further metabolized to the monophosphates" (BUA, 1992).

Conclusion.

In consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals, the Panel has conducted a thorough literature search for all available data, published and unpublished. It has performed an analysis of the adequacy of the existing data. Further, it developed a scientifically supportable category of related chemicals and used structure-activity relationship information to address certain requirements. The use of animals in this proposed test plan has been minimized.

Based upon the data provided in this report and the attached IUCLID documents, the physicochemical and toxicological properties of the PAD category members are similar and follow a regular pattern as a result of that structural similarity. Therefore, the EPA definition of a chemical category has been met.

All endpoints of the category have adequately satisfied requirements of the HPV Chemical Challenge Program, therefore additional tests are not proposed.

The summary endpoint matrix is included as **Table 5** of this document.

Introduction

A provision for the use of categories to reduce testing needs is included under EPA's HPV Program. Specifically, categories may be formed based on structural similarity, through analogy, or through a combination of category and analogy for use with single chemicals. The benefits of using a category approach are numerous and include: accelerated release of hazard information to the public; reduction in the number of animals used for testing; and an economic savings as a result of a reduced testing program.

The PAD chemicals that form this category, arranged in order of increasing molecular weight, are:

2-Ethylhexyl phosphate	**(12645-31-7)**
Dibutyl hydrogen phosphate	(107-66-4) *
Tributyl phosphate	(126-73-8) *
Bis (2-ethylhexyl) hydrogen phosphate	(298-07-7) *
Tris (2-ethylhexyl) phosphate	**(78-42-2)**

Two chemicals are sponsored by this Panel in the US EPA HPV Program. The chemicals marked with an asterisk (*) are included in support of the category, however are not being sponsored by this Panel. CAS # 107-66-4 and #126-73-8 have been assessed through the OECD SIDS Program. CAS# 298-07-7 will be sponsored by American Chemistry Council's HERTG Panel in 2003.

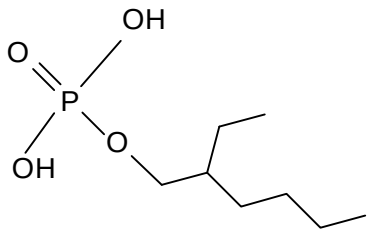
Development of the Phosphoric Acid Derivatives Category

EPA has described a stepwise process for developing categories. These steps include:

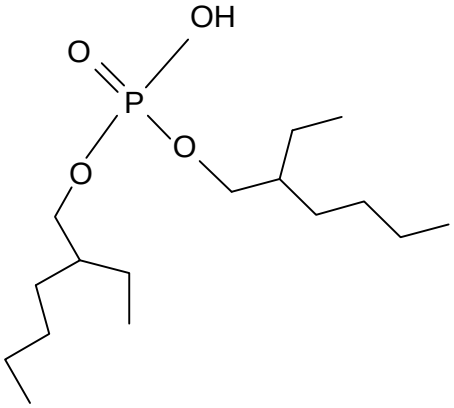
- Grouping a series of like chemicals, including the definition of criteria for the group.
- Gathering data on physicochemical properties, environmental fate and effects, and health effects for each member of the category.
- Evaluating the data for adequacy.
- Constructing a matrix of available and unavailable data.
- Determining whether there is a correlation among category members and data gathered.

Definition of the Phosphoric Acid Derivatives Category

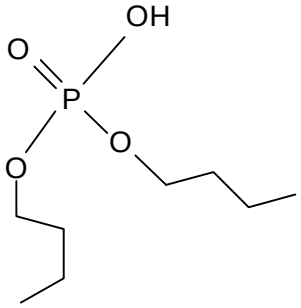
As defined by EPA under the HPV Program, a chemical category is "a group of chemicals whose physicochemical and toxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity." The similarities should be based on a common functional group, common precursors or breakdown products (resulting in structurally similar chemicals) and an incremental and constant change across the category. The goal of developing a chemical category is to use interpolation and/or extrapolation to assess chemicals rather than conducting additional testing.



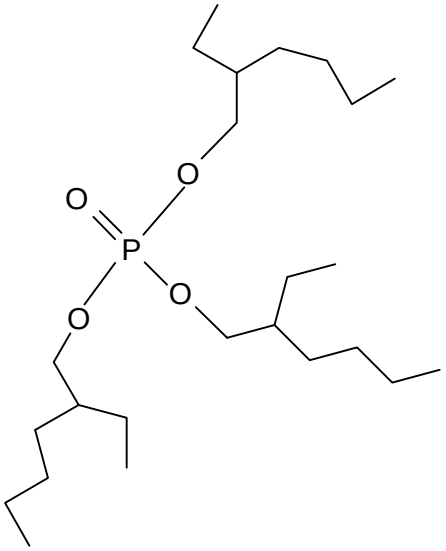
2-ethyl hexyl phosphate
CAS # 12645-31-7



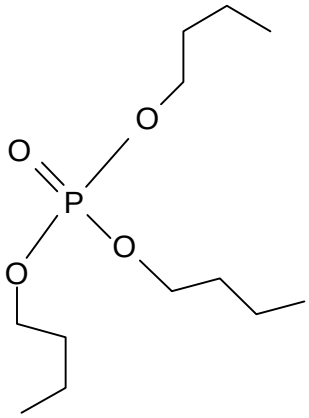
bis (2-ethyl hexyl) phosphate
CAS # 298-07-7



dibutyl hydrogen phosphate
CAS # 107-66-4



tris (2-ethyl hexyl) phosphate
CAS # 78-42-2



tributyl phosphate
CAS # 126-73-8

Figure 1. Chemical Structures

Structural Similarity.

A key factor supporting the classification of these chemicals as a category is their structural similarity. The chemicals within the PAD category are defined as esters of phosphoric acid, having a phosphoric acid backbone with various alkyl substituents as illustrated in **Figure 1**. The GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance reviewed the alkyl phosphate esters as a category in 1992 (BUA, 1992).

Metabolism.

"In mammalian metabolism, the phosphoric acid tri-esters are, as a rule, rapidly degraded to the corresponding di-ester. Only a small amount is further metabolized to the monophosphates." (BUA, 1992). In the case of tributyl phosphate, dibutyl hydrogen phosphate was the major metabolite (40-64% of the identified dose) and butyl dihydrogen phosphate was measured as 11-21% of the identified dose (Suzuki et al., 1984; IUCLID data set on CAS# 126-73-8).

Matrix of SIDS Endpoints

In order to construct a matrix of SIDS endpoints for the members of the PAD category, the data on physicochemical properties, environmental fate, ecotoxicity and health effects for each member of the category was collected and evaluated for adequacy. The results of these activities are presented in the tables and text below, as well as the attached IUCLID documents, providing a matrix of available data.

Correlation of Physicochemical Properties

The physicochemical properties of the members of the PAD category are presented in **Table 1**.
The PAD chemicals are non-flammable, colorless or pale colored liquids with low water solubility, very low vapor pressure and low partition coefficients. The similarities in the other physicochemical properties of these chemicals are explained by similarities in their chemical structure, and provide justification of this group of chemicals as a category within the HPV Challenge Program.

All members of the category have measured or calculated data on physicochemical properties. Data is available on all physicochemical endpoints for this category (See **Table 1**), therefore the requirements of the HPV Chemical Challenge Program have been adequately satisfied.

Correlation of Environmental Fate

The HPV Challenge Program requires that hydrolysis, photodegradation, biodegradation and environmental transport information be presented for each chemical or bridged to each member of a category. The EPIWIN modeling Program was used to calculate the photodegradation and fugacity for each chemical in the category. Two chemicals have been tested for photodegradation and there is good correlation with the calculated results. The members of this category have short photodegradation half-lives.

Adequate biodegradation data exist for four of the chemicals in this category; bridging will be used to fill the remaining requirement. Two chemicals (126-73-8 and 298-07-7) are categorized as "readily biodegradable" with degradation rates > 70% in the "ready test". Two chemicals (107-66-4 and 78-42-2) are regarded as "not readily biodegradable" with rates < 60% in the "closed bottle" test. The trend within the closed bottle tests clearly showed that the compound is metabolized slower as it becomes more polar. Thus, one could predict that the mono-ester would not be metabolized in the "closed bottle" system. The mono-ester (#12645-31-7) is expected to be "not readily biodegradable".

Partitioning to soil and sediment fractions (vs. water and air) is expected according to Fugacity Level III calculations. Default "input values" of 1000 kg/hr were used for the modeling.

Data is available or bridged for all Environmental Fate endpoints for this category (See **Table 2**), therefore the requirements of the HPV Chemical Challenge Program have been adequately satisfied.

Correlation of Ecotoxicity

The HPV Challenge Program requires that an acute aquatic toxicity test in fish, invertebrates, and algae be performed or bridged to each member of a category. Existing data indicate that the members of the PAD category have low water solubility. The low water solubility suggests that the acute aquatic toxicity of these chemicals should be low due to limited bioavailability to aquatic organisms. In general, data and modeling (ECOSAR) results support the low toxicity of PAD chemicals to aquatic organisms (See **Table 3**).

Data for the bis- and tris-(2-ethyl hexyl) esters demonstrate 96 hr Acute Fish LC_{50} from 30 mg/l to >100 mg/l. ECOSAR estimation for CAS#12645-31-7 is in line with the measured data.

Calculated and actual data for the mono- and bis-(2-ethyl hexyl) esters demonstrate 48 hr Acute Invertebrate LC_{50} to be >42 mg/l. Since the mono phosphate is expected to be more toxic than the tris-ester, the acute *Daphnia* LC_{50} of tris-(2-ethyl hexyl) phosphate is predicted to be >42 mg/l.

Acute toxicity to algae has been tested for 2-ethyl hexyl phosphate (12645-31-7) and demonstrated an EC_{50} of 161-168 mg/l. Since the mono phosphate is expected to be more toxic than the bis- and tris-esters, the EC_{50} of the tris-ester is expected to be greater than or equal to 161 mg/l.

No additional aquatic toxicity tests are proposed for this category as data is available or bridged for all endpoints (See **Table 3**). The requirements of the HPV Chemical Challenge Program have been adequately satisfied.

Correlation of Health Effects

Acute Mammalian Toxicity

Acute oral, dermal and inhalation toxicity data for the category is summarized in **Table 4**. Of the chemicals tested, all show a very low order of toxicity following oral or dermal administration. Although not all reports are GLP, may not follow OECD Guidelines, or may not be "robust" in their summaries, the "weight of evidence" demonstrates the low concern for acute toxicity.

The similarity in the order of toxicity for these chemicals is consistent with their similar chemical structure, metabolism, and physicochemical properties and supports the scientific justification of these chemicals as a category within the HPV Challenge Program. The acute oral LD_{50} of 2-Ethyl hexyl phosphate (12645-31-7) is expected to be about 2000 mg/kg bw in rats , which is similar to the acute toxicity of Dibutyl hydrogen phosphate (107-66-4) of same molecular weight.
The dermal LD50 for tributyl phosphate and tris(2-ethyl hexyl) phosphate are > 10,000 mg/kg bw. It is predicted that the acute dermal toxicity of 2-ethyl hexyl phosphate will also be in the non-toxic range.

The HPV Challenge Program requires that either an acute test be performed or bridged to each member of a category. Adequate acute oral toxicity tests exist for four of the five PAD chemicals. By bridging existing data to the one chemical where no data was found, the requirements of the HPV Challenge Program with respect to acute toxicity endpoints has been met, and no additional acute toxicity testing is proposed**.**

Repeat Dose Toxicity

A summary of the repeat dose toxicity data for the PAD category is presented in **Table 4**.

Repeat dose studies (28 D and/or 90 D studies) have been conducted with three of the PAD chemicals and demonstrate an apparent reduction in toxicity with increasing molecular weight. The repeat dose toxicity of 2-ethyl hexyl phosphate (12645-31-7) is expected to be similar to the repeat dose toxicity of Dibutyl hydrogen phosphate (107-66-4) of same molecular weight. The 44 day oral exposure NOAEL of Dibutyl hydrogen phosphate is 30 mg/kg bw in rats.

By bridging existing data to the one chemical where no data was found, the requirements of the HPV Challenge Program with respect to the repeat dose toxicity endpoint has been met, and no additional repeat dose toxicity testing is proposed**.**

Mutagenicity

A summary of the mutagenicity information for the PAD category is presented in **Table 4**. The weight of evidence for the members of this category indicates these chemicals are not mutagenic or clastogenic.

The HPV Challenge Program requires that adequate bacterial mutagenicity tests and *in vitro* chromosome aberration tests or *in vivo* micronucleus tests be performed or bridged to each member of a category. Adequate bacterial mutagenicity tests exist for four of the five PAD chemicals, and adequate *in vitro* or *in vivo* mammalian studies exist for three of the five chemicals. By bridging existing data to the one chemical where no data was found, the requirements of the HPV Challenge Program with respect to the mutagenicity endpoint has been met, and no additional mutagenicity testing is proposed**.**

Reproductive and Developmental Toxicity.

A summary of the reproductive and developmental toxicity data for the PAD category is presented in **Table 4**.

Adequate reproductive and developmental studies are available for two of the lower molecular weight chemicals in this category. These studies indicate an absence of reproductive or developmental effects of

these chemicals at doses ranging from >225 to 1000 mg/kg. Since repeat dose testing of this category demonstrates an apparent reduction in toxicity with increasing molecular weight, bridging existing data to the chemicals were no data was found is acceptable. No reproductive or developmental effects of 2-ethyl hexyl phosphate (12645-31-7) or tris (2-ethyl hexyl) phosphate (78-42-2) is expected at doses ranging from >225 to 1000 mg/kg.
By bridging existing data to the chemicals where no data was found, the reproductive and developmental toxicity aspect of this category has been evaluated adequately, meeting the requirements of the HPV Challenge Program and no additional reproductive and developmental toxicity testing is proposed**.**

Summary Endpoint Matrix / Test Plan

All endpoints of the category have been adequately characterized, meeting the requirements of the HPV Challenge Program, therefore additional tests are not proposed. A summary endpoint matrix is included as **Table 5** of this document.

Background Information: Manufacturing and Commercial Applications

Manufacturing

Tris (2-ethyl hexyl) phosphate (78-42-2) is produced by the reaction of phosphorus oxychloride with 2-ethyl hexanol followed by removal of hydrogen chloride co-product and typically further purification steps.

Commercial Applications

PAD chemicals are used as flame retardant plasticizers for polyvinylchloride resins, cellulose esters, lacquers and plastics, contributing flexibility and resistance to degradation at low temperatures, as solvents in liquid-liquid extractions, and as intermediates for wetting agents and detergents, as well as anti-foaming agents. They are used extensively as dispersing agents in plastisols, as catalysts in the manufacture of phenolic and urea resins, and in metal separation and extraction. These chemicals are also used as heat exchange mediums. (2000 Chemical Economics Handbook)

Shipping/Distribution

PAD chemicals are shipped extensively throughout the world from manufacturing plants.

Worker/Consumer Exposure

The Phosphoric Acid Derivatives industry has a long safety record and sophisticated users handle these chemicals. Exposure of workers handling PAD materials is likely to be highest in the area of packaging. These materials are liquids of very low vapor pressure, thus during the packaging process there is a low potential for inhalation exposure; an exposure of workers - if any- could take place by inhalation of very small droplets. Depending on handling procedures and filling equipment, dermal contact to the liquid is also possible.

Table 1. Matrix of Available and Adequate Data on the Phosphoric Acid Derivatives Category Physico-chemical Properties

Chemical **CAS#**	**2-Ethyl hexyl phosphate** **12645-31-7**	**Dibutyl hydrogen phosphate** **107-66-4**	**Tributyl phosphate** **126-73-8**	**Bis (2-ethyl hexyl) phosphate** **298-07-7**	**Tris (2-ethyl hexyl) phosphate** **78-42-2**
Molecular Weight:	210.21	210.21	266.32	322.43	434.65
Physical State	Colorless liquid	Pale, amber liquid	Colorless liquid	amber liquid	Colorless liquid
Melting Point	81.3ºC (EPI)	-13ºC 59.33ºC (EPI)	< -70ºC 64.73 ºC (EPI)	-50ºC 86.3ºC (EPI)	< -70ºC 87ºC (EPI)
Boiling Point	(decomp) 354ºC @1013 hPa (EPI)	>200ºC @20 hPa 319ºC @1013 hPa (EPI)	130ºC @ 5 hPa 327ºC @1013 hPa (EPI)	240ºC @ 1013 hPa (decomp) 400ºC @1013 hPa (EPI)	>210ºC @ 5 hPa (decomp) 446ºC @1013 hPa (EPI)
Relative Density	1.05 g/cm^3 @ 20ºC	1.05 g/cm^3 @ 20ºC	0.97 g/cm^3 @ 20ºC	0.96 g/cm^3 @ 20ºC	0.92 g/cm^3
Vapor Pressure	7.12 x10(-7)hPa @25ºC (EPI)	2.42 x 10(-5) hPa @25ºC (EPI) < .1 hPa at 20 º C	3.47 x 10(-6) hPa @25ºC	6.199 x10(-8) hPa @25ºC (EPI)	2.05 x 10(-7)hPa @25ºC (EPI)
Partition Coefficient (logP_{ow})	2.65 (EPI)	0.6-1.4 2.2 (EPI)	2.5 3.8 (EPI)	4.6-5.4 (ClogP) 6.071 (EPI)	4.2 9.49 (EPI)
Water Solubility	Dispersable 211 mg/l @25ºC (EPI)	18 g/l @20ºC 430 mg/l @25ºC (EPI)	0.4 g/l @20ºC 7.35 mg/l @25ºC (EPI)	< 1 g/l 0.059 mg/l @25ºC (EPI)	2 mg/l < 0.01 mg/l @25ºC (EPI)

= Non-sponsored chemicals used for data purposes only

EPI = EPIWIN modeling Program. Meylan, W. and Howard, P. (1999)

Table 2. Matrix of Available and Adequate Data on the Phosphoric Acid Derivatives Category Environmental Fate

Endpoint	**2-Ethyl hexyl phosphate 12645-31-7**	**Dibutyl hydrogen phosphate 107-66-4**	**Tributyl phosphate 126-73-8**	**Bis (2-ethyl hexyl) phosphate 298-07-7**	**Tris (2-ethyl hexyl) phosphate 78-42-2**
Photodegradation	T ½ = 3.9 hrs (AOP)	T ½ = 2.4 hrs (AOP)	T ½ = 1.6 hrs (AOP) 85% after 1 hr (UV)	T ½ = 2 hrs (AOP)	T ½ = 1.3 hrs (AOP) 80% after 1 hr (UV)
Hydrolysis	Not soluble enough to test	No data found	No hydrolysis after 30 D at any pH	No data found	No data found
Biodegradation	No data found	12% after 28D	77-92% after 28 D	0% after 5 D 75% after 28D (related to O_2 demand)	0% after 28 D
Fugacity Level III			(Level I)		
Air (%)	<0.1	0.183	.0737 (11)	0.278	0.312
Water (%)	29	34.4	41 (58)	12.9	10.9
Soil (%)	70.8	65.3	56.7 (16)	36.7	31.2
Sediment (%)	0.188	0.112	1.52 (15)	50.1	57.6

= Non-sponsored chemicals used for data purposes only

AOP = AOP Program, version 1.89. EPIWIN modeling Program.
Meylan, W. and Howard, P. (1999)

Table 3. Matrix of Available and Adequate Data on the Phosphoric Acid Derivatives Category Ecotoxicity

Endpoint	**2-Ethyl hexyl phosphate** **12645-31-7**	**Dibutyl hydrogen phosphate** **107-66-4**	**Tributyl phosphate** **126-73-8**	**Bis (2-ethyl hexyl) phosphate** **298-07-7**	**Tris (2-ethyl hexyl) phosphate** **78-42-2**
Acute Fish Toxicity 96 hr LC50	Freshwater fish = **38 mg/l** (ECOSAR)	*B. rerio* = **>100 mg/l** *B. rerio* = **>10,000mg/l**	*O. mykiss* = **13 mg/l** *B. rerio* = **10-14 mg/l**	*B. rerio* = **>56 mg/l** *S. gairdneri* = **30 mg/l**	*B. rerio* = **>100 mg/l** *O. latipes* = **>500 mg/l** (48 hr)
Acute Invertebrate Toxicity 48 hr EC50	*D. magna* = **42.7 mg/l** (ECOSAR)	*D. magna* = **90.9 mg/l** (ECOSAR)	*D. magna* = **2.6 – 9.0 mg/l**	*D. magna* = **> 42 mg/l**	No data found
Algal Toxicity 96 hr EC50	*S. capricornutum* = **161 - 168 mg/l** (72 hr) Green algae = 27.759 mg/l (ECOSAR)	Green algae = **57.8 mg/l** (ECOSAR)	*S. capricornutum* = **4.4 mg/l**	No data found	No data found

= Non-sponsored chemicals used for data purposes only

ECOSAR = ECOSAR v0.99e. EPIWIN modeling Program. Meylan, W. and Howard, P. (1999)

Table 4. Matrix of Available and Adequate Data on the Phosphoric Acid Derivatives Category Mammalian Toxicity

Endpoint	2-Ethyl hexyl phosphate 12645-31-7	Dibutyl hydrogen phosphate 107-66-4	Tributyl phosphate 126-73-8	Bis (2-ethyl hexyl) phosphate 298-07-7	Tris (2-ethyl hexyl) phosphate 78-42-2
Acute Toxicity					
Oral LD50	No data found	**2000 mg/kg bw** (rat)	**1390-11,265 mg/kg bw** (rat)	**4940 mg/kg bw** (rat)	**>36,800 mg/kg bw** (rat) **46,000 mg/kg bw** (rabbit)
Dermal LD50	No data found	No data found	**>3,100 - >10,000 mg/kg bw** (rabbit)	No data found	**~20,000 mg/kg bw** (rabbit)
Inhalation LC50	No data found	No data found	**>4.242 mg/l** (4 hr) (rat) **>42 mg/l** (6 hr) (rat)	No data found	**>0.447 mg/l** (4 hr) (rat)
Repeated Dose NOAEL=	No data found	**30 mg/kg** (oral – rat- 44 D)	**75 mg/kg bw** (female) **15 mg/kg bw** (male) (oral – rats -13 wk)	No data found	**1000 mg/kg bw** (oral - rat -13 wk) **430 mg/kg bw** (oral- rat - 30 D) **1.6 mg/m^3** (inhal. -g.pig- 90D)
Mutagenicity – gene mutation	No data found	Ames – negative	Ames – negative (5 studies - negative 1 study = positive) *E. coli* - negative Gene mutation (CHO cells) - negative	Ames – negative	Ames – negative mouse lymphona assay – negative
Mutagenicity – chromosome aberration	No data found	Chrom Aber. (CHL cells) – negative Micronucleus test (mouse)- negative	Chrom Aber. (CHO cells) – negative In vivo Cytogenetic assay (rat) – negative Drosophila SLRL - negative	No data found	Chrom Aber. (CHO cells) – negative Sister chromatid exchange - negative
Reproductive Toxicity	No data found	No effects on repro parameters up to **1000mg/kg bw** (oral – rat)	No effects on repro parameters up to **225 mg/kg bw** (oral – rat)	No data found	No data found
Developmental Toxicity NOAEL =	No data found	**300 mg/kg bw** (oral – rat) (Repro study)	**>250 mg/kg bw** (oral – rat)	No data found	No data found

= Non-sponsored chemicals used for data purposes only

Table 5. Summary of data for the Phosphoric Acid Derivatives Category

Endpoint	2-Ethyl hexyl phosphate 12645-31-7	Dibutyl hydrogen phosphate 107-66-4	Tributyl phosphate 126-73-8	Bis (2-ethyl hexyl) phosphate 298-07-7	Tris (2-ethyl hexyl) phosphate 78-42-2
Environmental Fate					
Photodegradation	C	C	A	C	A
Hydrolysis	A	NR	A	NR	R
Biodegradability	R	A	A	A	A
Fugacity	C	C	C	C	C
Ecotoxicology					
Acute Fish Toxicity	C	A	A	A	A
Acute Invertebrate Toxicity	C	C	A	A	R
AlgaL Toxicity	A	C	A	NR	R
Mammalian Toxicology					
Acute Toxicity	R	A	A	A	A
Mutagenicity – gene mutation	R	A	A	A	A
Mutagenicity – chromosome aberration	R	A	A	NR	A
Repeated Dose	R	A	A	NR	A
Reproductive Toxicity	R	A	A	NR	R
Developmental Toxicity	R	A	A	NR	R

Key for symbols in table:
A = Adequate data available
R = Endpoint requirement fulfilled using category approach, SAR
C = Endpoint requirement fulfilled based on calculated data
NR = No testing required; chemical not sponsored

= Non-sponsored chemicals used for data purposes only.

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